



PATENT

Case Docket No. NEREUS.2C1CP1

Date: April 6, 2004

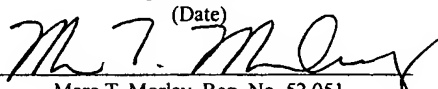
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s) : Hayashi, et al.  
Appl. No. : 10/632,688  
Filed : August 1, 2003  
For : PHENYLHISTIN AND THE  
PHENYLHISTIN ANALOGS,  
A NEW CLASS OF ANTI-  
TUMOR COMPOUNDS  
Examiner : Unknown  
Group Art Unit : 1614

I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on

April 6, 2004

(Date)

  
Marc T. Morley, Reg. No. 52,051


TRANSMITTAL LETTER

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Enclosed for filing in the above-identified application are:

- (X) A Supplemental Information Disclosure Statement.
- (X) A PTO Form 1449 listing forty-seven (47) references, which are included herewith.
- (X) Power of Attorney from Nereus Pharmaceuticals, Inc., in 2 pages, with attached copy of assignment in 2 pages.
- (X) The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Account No. 11-1410.
- (X) Return prepaid postcard.

  
Marc T. Morley  
Registration No. 52,051  
Attorney of Record  
Customer No. 20,995  
(619) 235-8550



## SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Applicant : Hayashi, et al.  
App. No. : 10/632,688  
Filed : August 1, 2003  
For : PHENYLAHISTIN AND THE  
PHENYLAHISTIN ANALOGS, A NEW  
CLASS OF ANTI-TUMOR COMPOUNDS  
Examiner : Unknown  
Group Art Unit : 1614

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Enclosed is form PTO-1449 listing 47 references that are also enclosed.

This Information Disclosure Statement is being filed before the receipt of a first Office Action on the merits, and presumably no fee is required in accordance with 37 C.F.R. § 1.97(b)(3). If a first Office Action on the merits was mailed before the mailing date of this Statement, the Commissioner is authorized to charge the fee set forth in 37 C.F.R. § 1.17(p) to Deposit Account No. 11-1410.

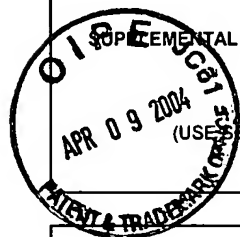
Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 4/6/04

By: M. T. Morley  
Marc T. Morley  
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FORM PTO-1449

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.  
NEREUS.2C1CP1APPLICATION NO.  
10/632,688SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT  
BY APPLICANT

(USE SEVERAL SHEETS IF NECESSARY)

APPLICANT  
Hayashi, et al.FILING DATE  
August 1, 2003GROUP  
1614

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE (IF APPROPRIATE)

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	1	JP10130266	05/19/98	Japan			X (Abstract)	

EXAMINER INITIAL	OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)	
	2	Ahmed, S.A. et al. "A new rapid and simple non-radioactive assay to monitor and determine the proliferation of lymphocytes: an alternative to [ <sup>3</sup> H]thymidine incorporation assay." <i>J. Immunol. Methods</i> . 170, 211-224 (1994).
	3	Algaier, J. et al. "The effects of dimethyl sulfoxide on the kinetics of tubulin assembly." <i>Biochim. Biophys. Acta</i> . 954, 235-43 (1988).
	4	Ali M. et al. "Toxicity of echinulin from <i>Aspergillus chevalieri</i> in rabbits." <i>Toxicology Letters</i> . 48, 235-41 (1989).
	5	Bond, R., et al. "The Synthesis of Viridamine, a <i>Penicillium Viridicatum</i> Mycotoxin." <i>Synthetic Commun</i> . 19 (13&14), 2551-2566 (1989).
	6	Borisy, G.G. "A Rapid Method for Quantitative Determination of Microtubule Protein using DEAE-Cellulose Filters." <i>Anal. Biochem</i> . 50, 373-385 (1972).
	7	Cui, C. et al. "Novel Mammalian Cell Cycle Inhibitors, Tryprostatins A, B and Other Diketopiperazines Produced by <i>Aspergillus fumigatus</i> ." <i>J. Antibiotics</i> . 49, 534-40 (1996).
	8	Cui, C. et al. "Novel Mammalian Cell Cycle Inhibitors, Tryprostatins A, B and Other Diketopiperazines Produced by <i>Aspergillus fumigatus</i> ." <i>J. Antibiotics</i> . 49, 527-33 (1996).
	9	Goldani, L.Z. & Sugar, A.M. "Treatment of murine pulmonary mucormycosis with SCH 42427, a broad-spectrum triazole antifungal drug." <i>J Antimicrob Chemother</i> . 33, 369-372 (1994).
	10	Gordon, D., et al. "Reductive Alkylation on a Solid Phase: Synthesis of a Piperazinedione Combinatorial Library." <i>J. Bioorg. Med. Chem. Letters</i> . 5, 47-50 (1995).
	11	Hamel, E. "Antimitotic Natural Products and Their Interactions with Tubulin." <i>Med. Res. Rev.</i> 16(2), 207-31 (1996).
	12	Hartwell, L.H. et al. "Checkpoints: Controls that Ensure the Order of Cell Cycle Events." <i>Science</i> . 246, 629-34 (1989).

EXAMINER

DATE CONSIDERED

\*EXAMINER: INITIAL IF CITATION CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP 609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED, INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.

FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. NEREUS.2C1CP1	APPLICATION NO. 10/632,688
SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (USE SEVERAL SHEETS IF NECESSARY)		APPLICANT Hayashi, et al.	
		FILING DATE August 1, 2003	GROUP 1614

EXAMINER INITIAL	OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)	
	13	Horak R.M. et al. "Structures of the Austalides A-E, Five Novel Toxic Metabolites from <i>Aspergillus ustus</i> ." <i>J.C.S. Chem. Comm.</i> 1265-67 (1981).
	14	Iwasaki, S. "Bioactive Natural Products Interfering with Microtubule Function." <i>Kagaku to Seibutsu.</i> 32(3), 153-159 (1994).
	15	Iwasaki, S. "Antimitotic Agents: Chemistry and Recognition of Tubulin Molecule." <i>Med Res Rev.</i> 13,183-198 (1993).
	16	Johnson, K.A. et al. "Kinetic Analysis of Microtubule Self-assembly in Vitro." <i>J. Mol. Biol.</i> 117, 1-31 (1977).
	17	Keepers Y.P., et al. "Comparison of the Sulforhodamine B Protein and Tetrazolium (MTT) Assays for in vitro Chemosensitivity Testing." <i>Eur. J. Cancer.</i> 27, 897-900 (1991).
	18	Kondoh, M. et al. "Effects of Tryprostatin Derivatives on Microtubule Assembly In Viro and In Situ." <i>J. Antibiotics.</i> 51, 801-04 (1998).
	19	Krishan, A. "Rapid Flow Cytofluorometric Analysis of Mammalian Cell Cycle By Propidium Iodide Staining." <i>J. Cell Biol.</i> 66, 188-193 (1975).
	20	Kupchan, S.M. et al. "Steganacin and Steganangin, Novel Antileukemic Lignan Lactones from <i>Steganotaenia araliacea</i> 1-3." <i>J. Am. Chem. Soc.</i> 95(4), 1335-36 (1973).
	21	Lacey, E. et al. "Interaction of Phomopsin A and Related Compounds with Purified Sheep Brain Tubulin." <i>Biochem. Pharmacol.</i> 36, 2133-38 (1987).
	22	Laemmli, U.K. "Cleavage of Structural Proteins during the Assembly of the Head of Bacteriophage T4." <i>Nature.</i> 227, 680-85 (1970).
	23	Larsen, T.O et al. "Aurantiamine, A Kiketopiperazine from Two Varieties of <i>Penicillium Aurantiogriseum</i> ." <i>Phytochemistry.</i> 31, 1613-1615 (1992).
	24	Lee, J.C. et al. "The Reconstitution of Microtubules from Purified Calf Brain Tubulin." <i>Biochemistr.</i> 14(23), 5183-87 (1975).
	25	Li, Y., et al. "Interaction of marine toxin dolastatin 10 with porcine brain tubulin: competitive inhibition of rhizoxin and phomopsin A binding." <i>Chem. Biol. Interact.</i> 93, 175-83 (1994).
	26	Liwo, A. et al. "Origin of the Ring-Ring Interaction in Cyclic Dipeptides Incorporating an Aromatic Amino Acid." <i>Tetrahedron Lett.</i> 26, 1873-1876 (1985).
	27	Ludueno, R.F. "Contrasting Roles of Tau and Microtubule-associated Protein 2 in the Vinblastine-induced Aggregation of Brain Tubulin." <i>J. Biol. Chem.</i> 259:12890-98 (1984).
	28	Pettit, G.R. et al. "Antineoplastic Agents. 291. Isolation and Synthesis of Combretastatins A-4, A-5, and A-6 1a." <i>J. Med. Chem.</i> 38, 1666-1672 (1995).
	29	Roberge, M. et al. "Antitumor Drug Fostriecin Inhibits the Mitotic Entry Checkpoint and Protein Phosphatases 1 and 2A." <i>Cancer Res.</i> 54, 6115-21 (1994).
	30	Rowinsky, E. K. et al. "Taxol: A Novel Investigational Antimicrotubule Agent." <i>J. Natl. Cancer Inst.</i> 82, 1247-59 (1990).
	31	Sackett, D.L. "Podophyllotoxin, Steganacin and Combretastatin: Natural Products that Bind at the Colchicine Site of Tubulin." <i>Pharmacol. Ther.</i> 59, 163-228 (1993).

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	32	Sherline, P., et al. "Binding of Colchicine to Purified Microtubule Protein." <i>J. Biol. Chem.</i> 250, 5481-86 (1975).
	33	Smedsgaard J. et al. "Using direct electrospray mass spectrometry in taxonomy and secondary metabolite profiling of crude fungal extracts." <i>J. Microbiol. Meth.</i> 25, 5-17 (1996).
	34	Steyn, P.S. "The Structures of Five Diketopiperazines from <i>Aspergillus Ustus</i> ." <i>Tetrahedron.</i> 29, 107-120 (1973).
	35	Sugar, A., et al. "Comparison of Three Methods of Antifungal Susceptibility Testing with the Proposed NCCLS Standard Broth Macrodilution Assay: Lack of Effect of Phenol Red." <i>Diagn Micro and Infect Diseases.</i> 21, 129-133 (1995).
	36	Takahashi, M., et al. "Rhizoxin binding to tubulin at the maytansine-binding site." <i>Biochim. Biophys. Acta.</i> 926, 215-23 (1987).
	37	Tiwari, S.C. et al. "A pH- and Temperature-Dependent Cycling Method that doubles the Yield of Microtubule Protein." <i>Anal. Biochem.</i> 215, 96-103 (1993).
	38	Turner and Rodriguez. "Recent Advances in the Medicinal Chemistry of Antifungal Agents." <i>Current Pharmaceutical Design.</i> 2, 209-224 (1996).
	39	Usui, T. et al. "Tryprostatin A, a specific and novel inhibitor of microtubule assembly." <i>Biochem J.</i> 333, 543-48 (1998).
	40	Van der Waerden, B.L. <i>Arch Exp Pathol Pharmacol.</i> 195, 389-412, (1940).
	41	Verdier-Pinard, P., et al., "Structure-Activity Analysis of the Interaction of Curacin A, the Potent Colchicine Site Antimitotic Agent, with Tubulin and Effects of Analogs on the Growth of MCF-7 breast Cancer Cells." <i>Mol. Pharmacol.</i> , 53, 62-76 (1998).
	42	Weisenberg, R.C. et al. "The Colchicine-Binding Protein of Mammalian Brain and its Relation to Microtubules." <i>Biochemistry</i> 7(12), 4466-79 (1968).
	43	Yahara, I. et al. "Microtubule Organization of Lymphocytes and its Modulation by Patch and Cap Formation." <i>Cell.</i> 15, 251-259 (1978).
	44	Yamazaki, M. et al. "Crystal Structure and Absolute Configuration of Fumitremorgin B, a Tremorgenic Toxin from <i>Aspergillus Fumigatus</i> Fres." <i>Tetrahedron Lett.</i> 1, 27-28 (1975).
	45	Yamori T. <i>Jap. J. Cancer Chemother.</i> 24, 129-35 (1997).
	46	Yoshida, Minoru M. <i>Protein Nucleic Acid Enzymes.</i> 38, 1753-1765 (1993).
	47	Yoshimatsu, K., et al. "Mechanism of Action of E7010, an Orally Active Sulfonamide Antitumor Agent: Inhibition of Mitosis by Binding to the Colchicine Site of Tubulin." <i>Cancer Res.</i> 57, 3208-13 (1997).

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